REMARKS/ARGUMENTS

Claims 76-96 are pending, Claims 1-12 have been withdrawn, and Claims 13-75 have been cancelled.

Claims 76-96 and withdrawn Claims 1-12 have been amended to recite that the host cells are diminished or depleted in the activity of an initiating α-1,6-mannosyltransferase and includes at least an α-1,2-mannosidase activity and a GlcNAc transferase I (GnT I) activity. Support for this amendment can be found throughout the specification and in the examples. In particular, Example 19, which exemplifies host cells engineered to produce $GlcNAcMan_5GlcNAc_2$ (strain YSH-1) and which produce N-glycans having the $GlcNAcMan_5GlcNAc_2$ glycoform. YSH-1 cells are capable of producing the $GlcNAcMan_5GlcNAc_2$ structure because the cells include an *OCH1* deletion to render the cells deficient in initiating α-1,6-mannosyltransferase activity, alpha-1,2-mannosidase I, GnT I, and a GlcNAc transporter. Figures 26-28 shows MALDI-TOF results showing that the N-glycans produced in yeast cells that produce $GlcNAcMan_5GlcNAc_2$ and which further include a nucleic acid that expresses GnT III, produce N-glycans having a bisected $GlcNAc_2Man_5GlcNAc_2$ glycoform.

Examples 20 and 21 exemplify host cells engineered to produce $GlcNAc_2Man_3GlcNAc_2$ (strains YSH-44 and PBP6-5) and which produce N-glycans having the $GlcNAc_2Man_3GlcNAc_2$ glycoform. YSH-44 cells are capable of producing the $GlcNAc_2Man_3GlcNAc_2$ structure because the cells include an *OCH1* deletion, alpha-1,2-mannosidase I activity, GnT I activity, mannosidase II activity, GnT II activity, and a GlcNAc transporter. PBP6-5 cells are capable of producing the $GlcNAc_2Man_3GlcNAc_2$ structure because the cells include an *OCH1* deletion, an *Alg3* deletion, alpha-1,2-mannosidase I activity, GnT I activity, GnT II activity, and a GlcNAc transporter. Figures 30 and 32 show that when the host cells further include a nucleic acid that expresses GnT III (strains YSH-57 and PBP38, respectively), they produce N-glycans having a bisected $GlcNAc_3Man_3GlcNAc_2$ glycoform.

Withdrawn Claims 1-12 have further been amended to recite that the host cells are "yeast" host cells. Withdrawn Claim 8 has also been amended to cancel non-yeast species. The amendment to withdrawn Claims 1-12 have been made in order to preserve the right of rejoinder of these non-elected Claims 1-12 with the elected claims, when allowed.

I. Claims 13-17, 22-24, 32, and 35-37 have been rejected under 35 U.S.C. § 112, first paragraph.

The rejection states that Claims 13-17, 22-24, 32, and 35-37 fail to comply with the written description requirement. Claims 13-17, 22-24, and 32-39 and Claims 55-75 have been cancelled without prejudice. Therefore, the rejection to these claims is now moot.

II. Claims 76-96 have rejected under 35 U.S.C. § 112, first paragraph.

The rejection states that Claims 76-96 fail to comply with the written description requirement and specifically states "As indicated in the instant specification and response filed on 8/27/07, it is apparent that once a lower eukaryote host cell that is deficient in or lack alpha-1,6 mannosyltransferase activity has been obtained, the host cells can be further modified to include an alpha-1,2-mannosidase activity and a GnT I activity to produce a hybrid GlcNAcMan5GlcNAc2 N-glycan structure. As such, for a yeast cell comprising GnTIII activity only, it cannot produce complex or hybrid N-glycan. Since specification does not describe other types of engineering process without at least the introduction of an alpha-1,2mannosidase activity and a GnT I activity to produce the claimed yeast host cell, a representative number of species of the claimed yeast host cell have not been described. Therefore, this rejection also applies to these claims."

Claims 76, 81, 86, and withdrawn Claims 1, 2, and 3 have been amended to recite that the yeast host cell is diminished or depleted in the activity of an initiating α-1,6-mannosyltransferase and includes at least an α-1,2-mannosidase activity and a GlcNAc transferase I (GnT I) activity. This amendment specifies that the yeast host cells be deficient in or lack alpha-1,6 mannosyltransferase activity and to be further modified to include at least an alpha-1,2-mannosidase activity and a GnT I activity. As shown in Example 19, such yeast host cells, which produce hybrid $GlcNAcMan_5GlcNAc_2$ N-glycan structures, can produce bisected $GlcNAc_2Man_5GlcNAc_2$ N-glycan structures when transformed with a vector encoding a GnT III activity (strain PBP26). The addition of a mannosidase II and a GnT II to the above host cells or making an *alg3* inactivation and adding a GnT II to the above host cells produces host cells that can make a bisected $GlcNAc_2Man_3GlcNAc_2$ N-glycan structure when transformed with a vector that encodes a GnT III activity. Example 20 provides strain YSH-44, which is an OCH1 deficient strain that includes alpha-1,2-mannosidase activity, GnT I activity, a mannosidase II activity, and a GnT II activity and produces $GlcNAc_2Man_3GlcNAc_2$ N-glycan structures, produces bisected $GlcNAc_3Man_3GlcNAc_2$ N-glycan structures when transformed with a vector encoding GnT III. Example 21 shows that strain PBP6-5, which is an *OCH1* and *ALG3* deficient strain that includes an alpha-1,2-mannosidase activity, GnT I activity, and a GnT II activity,

produces bisected $GlcNAc_3Man_3GlcNAc_2$ N-glycan structures when transformed with a vector encoding a GnT III activity.

The applicants respectfully believe that currently amended Claims 76-96 comport with the written description requirement 35 U.S.C. § 112, first paragraph. In light of the current amendments to Claims 76, 81, and 86, reconsideration of the rejection is requested.

III. Objection to Amendment to the Specification

The amendment made to the specification in the amendment filed on 08/27/07 was objected to for disclosing new matter into the disclosure of the invention. The added matter was the cancellation of various elements in the definition of lower eukaryotes. While respectfully disagreeing with the objection, the cancelled material has been reintroduced into the specification in this amendment.

In light of the above, reconsideration of the objection is requested.

CONDITIONAL PETITION

Applicant hereby makes a Conditional Petition for any relief available to correct any defect in connection with this filing, or any defect remaining in this application after this filing. The Commissioner is authorized to charge deposit account 13-2755 for the petition fee and any other fee(s) required to effect this Conditional Petition.

Respectfully submitted,

By _____
John David Reilly
Reg. No. 43,039
Attorney for Applicant

MERCK & CO., INC.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-6914

Date: Feb 29, 2008